

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE  
in its capacity as elected Office

Date of mailing (day/month/year) 11 April 2002 (11.04.02)	
International application No. PCT/US00/20400	Applicant's or agent's file reference WFU 99-35
International filing date (day/month/year) 27 July 2000 (27.07.00)	Priority date (day/month/year) 27 July 1999 (27.07.99)
Applicant HART, Thomas, C.	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

27 February 2001 (27.02.01)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer N. Santesso Telephone No.: (41-22) 338.83.38
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10/031889 -

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 19 MAR 2002

WFO

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Applicant's or agent's file reference WFO 99-35	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/20400	International filing date (day/month/year) 27 JULY 2000	Priority date (day/month/year) 27 JULY 1999
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant WAKE FOREST UNIVERSITY		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 27 FEBRUARY 2001	Date of completion of this report 27 FEBRUARY 2002
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer <i>Joyce Bridges</i> Carla Myers
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/20400

## I. Basis of the report

1. With regard to the **elements** of the international application:\*

- ☒ the international application as originally filed
- ☒ the description:  
pages 1-71, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the claims:  
pages 72-79, as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the drawings:  
pages 1-9, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the sequence listing part of the description:  
pages NONE, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.  
These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/20400

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. statement

Novelty (N)

Claims	<u>1-41</u>	YES
Claims	<u>NONE</u>	NO

Inventive Step (IS)

Claims	<u>1-41</u>	YES
Claims	<u>NONE</u>	NO

Industrial Applicability (IA)

Claims	<u>1-41</u>	YES
Claims	<u>NONE</u>	NO

### 2. citations and explanations (Rule 70.7)

Claims 1-41 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the specifically claimed mutations in the CTSC gene. Accordingly, the prior art does not teach or suggest the claimed nucleic acids which specifically hybridize to the stated mutated CTSC nucleic acids and the prior art does not teach or suggest the specifically claimed proteins comprising mutated CTSC nucleic acid sequences or antibodies which are immunologically specific for said proteins.

\_\_\_\_\_ NEW CITATIONS \_\_\_\_\_  
NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/20400

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 13-37 and 40-41 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s):

Claims 13-37 are indefinite for failing to recite a final process step which agrees back with the preamble. The claims are drawn to methods for detecting a germline mutation. However, the claims recite only the step of analyzing a CTSC sequence. The claims do not set forth how the step of analyzing a CTSC sequence results in the detection of a germline mutation. Accordingly, it is unclear as to whether the claims are intended to be limited to methods for detecting a germline mutation or to methods for analyzing the sequence of a CTSC gene or mRNA.

Claims 40-41 are indefinite over the recitation of "CTSC proteins of the invention" because the claims do not clearly set forth which proteins are encompassed by the claims. The claims should be amended to refer to, for example, mutated CTSC proteins encoded by a mutated CTSC nucleic acid, wherein said nucleic acid contains a mutation as set forth in Table 1.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/20400

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:  
IPC(7): C12Q 1/68; C12P 19/34; C07H 21/04; C07K 14/435, 16/18; G01N 33/53 and US Cl.: 435/6, 7.1, 91.2; 536/23.5,  
24.31, 24.33; 530/350, 388.1

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: KATHLEEN D. RIGAUT  
DANN, DOREMAN, HERRELL AND SKILLMAN  
1601 MARKET STREET  
SUITE 720  
PHILADELPHIA, PA 19103-2307

## PCT

### NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing  
(day/month/year)

**14 MAR 2002**

Applicant's or agent's file reference

WFC 99-33

#### IMPORTANT NOTIFICATION

International application No.

PCT/US00/20400

International filing date (day/month/year)

27 JULY 2000

Priority Date (day/month/year)

27 JULY 1999

Applicant

WAKE FOREST UNIVERSITY

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US  
Commissioner of Patents and Trademarks  
Box ICT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

Carla Myers

Telephone No. (703) 308-1235

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/20400

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68; C12P 19/34; C07H 21/04; C07K 14/435, 16/18; G01N 33/53

US CL : 435/6, 7.1, 91.2; 536/23.5, 24.31, 24.33; 530/350, 388.1

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 7.1, 91.2; 536/23.5, 24.31, 24.33; 530/350, 388.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P ---- Y,P	TOOMES et al. Loss-of-function mutations in the cathepsin C gene result in periodontal disease and palmoplantar keratosis. Nature Genetics. December 1999, Vol. 23, pages 421-424, especially Table 2.	1, 2 ----- 11-24, 26, 35-41
X,P ---- Y,P	HART et al. Mutations of the cathepsin C gene are responsible for Papillon-Lefevre syndrome. Journal of Medical Genetics. December 1999, Vol. 36, pages 881-887, especially page 885.	1-3, 5-7 ----- 11-24, 26-27, 29-31, 35-41
X,P ---- Y,P	HART et al. Haim-Munk syndrome and Papillon-Lefevre syndrome are allelic mutations in cathepsin C. Journal of Medical Genetics. February 2000, Vol. 37, pages 88-94, especially pages 92-93.	1-4 ----- 11-24, 26-28, 35-41

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"A" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search  
27 NOVEMBER 2000

Date of mailing of the international search report

27 DEC 2000

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

Carla Myers

Telephone No. (703) 308-1235



# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/20400

## B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

WEST: US, EP, JP, WO Patents; DIALOG: Medline, CA, Biosis, Embase, SciSearch

search terms: CTSC or cathepsin C or dipeptidyl aminopeptidase and mutation or polymorphism or deletion

PCT

From the INTERNATIONAL BUREAU

**NOTICE INFORMING THE APPLICANT OF THE  
COMMUNICATION OF THE INTERNATIONAL  
APPLICATION TO THE DESIGNATED OFFICES**

(PCT Rule 47.1(c), first sentence)

To:

RIGAUT, Kathleen, D.  
Dann, Dorfman, Herrell and Skillman  
Suite 720  
1601 Market Street  
Philadelphia, PA 19103-2307  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 01 February 2001 (01.02.01)		
Applicant's or agent's file reference WFU 99-35		<b>IMPORTANT NOTICE</b>
International application No. PCT/US00/20400	International filing date (day/month/year) 27 July 2000 (27.07.00)	
Priority date (day/month/year) 27 July 1999 (27.07.99)		
Applicant WAKE FOREST UNIVERSITY et al		

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:  
AU,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:  
AE,AG,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,BZ,CA,CH,CN,CR,CU,CZ,DE,DK,DM,DZ,EA,EE,EP,ES,  
FI,GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,  
MN,MW,MX,MZ,NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU,  
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).
3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on  
01 February 2001 (01.02.01) under No. WO 01/07663

**REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)**

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

**REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))**

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer  J. Zahra  Telephone No. (41-22) 338.83.38
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# DANN, DORFMAN, HERRELL AND SKILLMAN

## A PROFESSIONAL CORPORATION

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COMMISSIONER OF PATENTS AND TRADEMARKS WASHINGTON, DC 20231	DATE OF MAILING  25 January 2002
BOX PCT	APPLICANT'S OR AGENT'S FILE REF. WFU.99-35
IDENTIFICATION OF THE INTERNATIONAL APPLICATION	
INTERNATIONAL APPLICATION NO. PCT/US00/20400	INTERNATIONAL FILING DATE 27 July 2000
APPLICANT (name) WAKE FOREST UNIVERSITY	
TRANSMITTAL OF LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)	

### CERTIFICATE OF MAILING BY EXPRESS MAIL UNDER 37 C.F.R. §1.10

NO. OF EXPRESS MAIL LABEL EL676443155US

DATE OF DEPOSIT WITH POSTAL SERVICE January 25, 2002

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. §1.10 on the date indicated above, and is addressed to the COMMISSIONER OF PATENTS, BOX PCT, Washington, DC 20231-0001.

Jane C. Bogan  
Name of Person Mailing Paper or Fee

Jane C. Bogan  
Signature of Person Mailing Paper or Fee